

Anemias

Learning Objectives

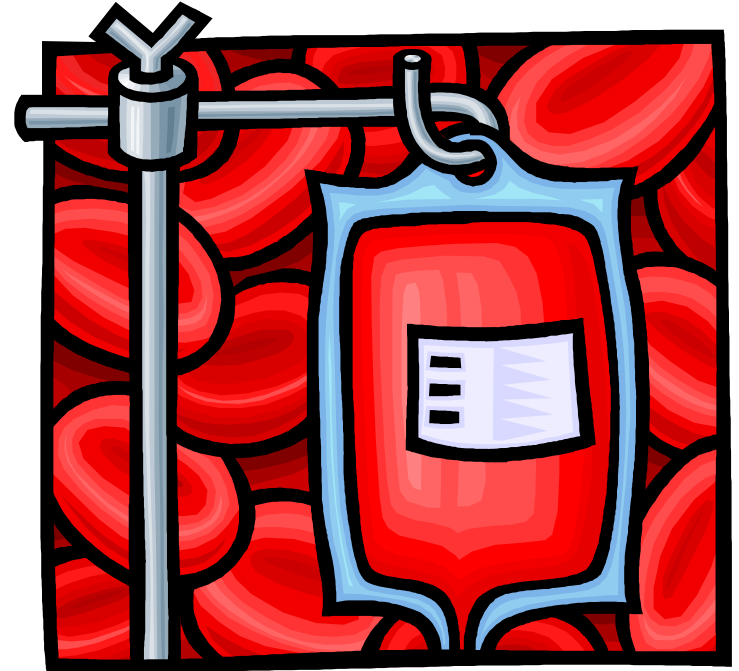
- **Define anemias.**
- **Describe the etiology, pathology, clinical features, diagnostic studies, and management of iron deficiency anemia, A- and B-Thalassemias, sickle cell anemia, aplastic anemia, and megaloblastic anemia.**

Learning Objectives

- **Identify the causes, diagnosis, and treatment of Vitamin B12 deficiency and total body folate deficiency.**
- **Describe the causes, clinical features, diagnosis and treatment of Glucose 6 Phosphate Dehydrogenase (G6PD) deficiency.**

Anemias

- Requirements each hour each day
 - 1.5×10^9 RBCs
 - 1.5×10^9 WBCs



Anemias

- **Process**
 - **Pluripotent hematopoietic stem cell differentiates into specialized blood cells (hematopoiesis or hemopoiesis)**

Anemias

**Pluripotent Hematopoietic
Stem cell**

**Lymphocytic
Progenitor Cells**

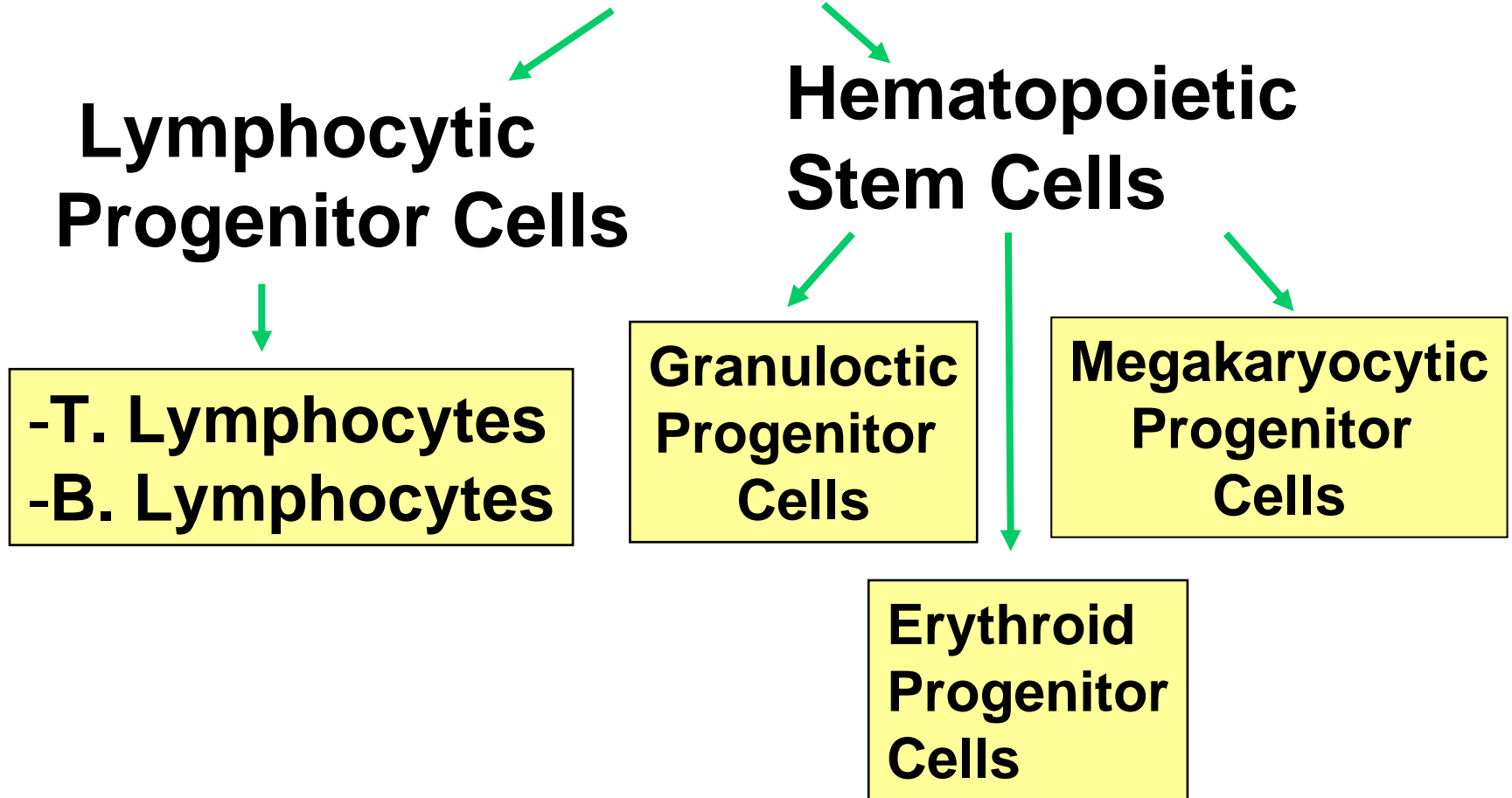
**Hematopoietic
Stem Cells**

**-T. Lymphocytes
-B. Lymphocytes**

**Granulocytic
Progenitor
Cells**

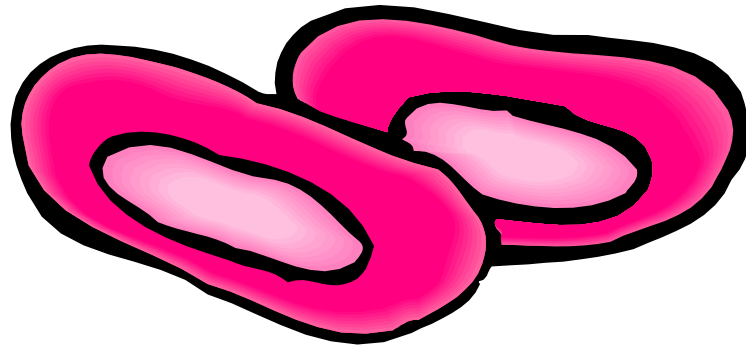
**Megakaryocytic
Progenitor
Cells**

**Erythroid
Progenitor
Cells**



Anemias

- **Anemia**
 - **Reduction in red cell mass**
 - **Reduction in the hemoglobin concentration**
 - **Homeostasis upset**



Red Blood Cell

Anemias

- **Possible etiologies**
 - **Primary derangement of the marrow**
 - **Accelerated loss of red blood cells peripherally**
 - **Systemic pathology**
- **Sign of underlying pathology**

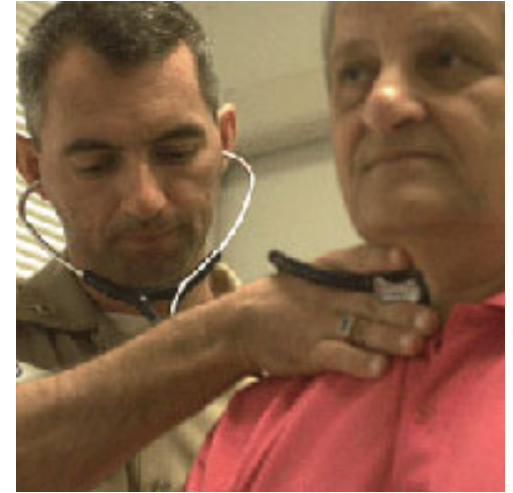
Anemias

- **Definition: Hematocrit or Hemoglobin < lower limit of normal**
 - **Men: Hematocrit <41% or Hemoglobin <13.5g/dL**
 - **Women: Hematocrit <36% or Hemoglobin <12g/dL**



Anemias - Evaluation

- Clinical manifestations
- Physical exam
- Family history
- Lab studies



Anemias - Evaluation

- **Clinical manifestations**
 - **Fatigue**
 - **Dyspnea**
 - **Lightheadedness**
 - **Decreased exercise tolerance**
 - **Headache**
 - **Angina**

Anemias - Evaluation

- **Physical exam**
- **Pallor**
- **Glossitis**
- **Jaundice**
- **Splenomegaly**
- **Neurological abnormalities**
- **Bone tenderness**
- **Hemoccult positive feces**

Anemias - Evaluation

- **Family history: Get details**
- **Lab studies**
 - **Reticulocyte Production Index (RPI)**
 - **Reticulocyte is early blood cell, 1-2 days old, released from bone marrow**

Anemias: Lab Studies

$$\text{Reticulocyte \% corrected} = \text{Retic\% reported} \times \frac{(\text{Pt Hematocrit})}{45}$$

then

$$\text{Reticulocyte Production Index (RPI)} = \frac{\text{Retic\% corrected}}{\text{Correction Factor}}$$

Anemias: Lab Studies

Patient Hct %

Correction factor

40-45%

1.0

35-39%

1.5

25-34%

2.0

15-25%

2.5

<15%

3.0

Anemias: Lab Studies

RPI = < 2.0 Inadequate bone marrow response (hypo-proliferation)

RPI = > 3.0 Appropriate bone marrow response

Anemias: Lab Studies

- **Other CBC parameters**
 - **WBC, platelets counts**
 - **Mean Corpuscular Volume (MCV): measure of av. RBC size or volume**
 - **Red Cell Distribution Width (RDW): RBC size generally not variable**

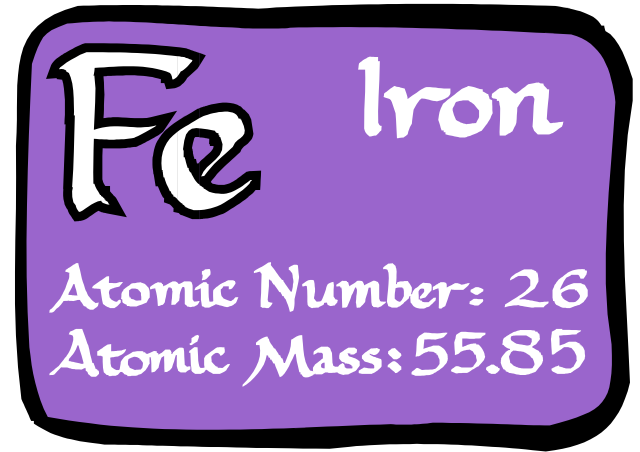
Anemias: Lab Studies

- **Peripheral Blood Smear**
 - **Inspect, describe, define any abnormalities**
- **Hemoccult**
 - **Do 3 times**
 - **If +, order colonoscopy / endoscopy**



Iron Deficiency Anemia

- Total body iron
- Adult males – 3800mg
- Adult females – 2500mg



Iron Deficiency Anemia

- **Iron pathway in the body**
 - **Iron in developing red blood cells**
 - **Old erythrocytes removed from circulation, iron freed from Hb, stored as ferritin/hemosiderin or released to transferrin**
 - **Iron bound to transferrin (plasma iron transporting protein) carried to bone marrow for uptake**

Iron Deficiency Anemia

- **Iron absorption**
 - **Duodenum, jejunum**
- **Sources of iron**
 - **Heme iron: Meat, fish, liver**
 - **Non-heme iron: Vegetables, legumes**



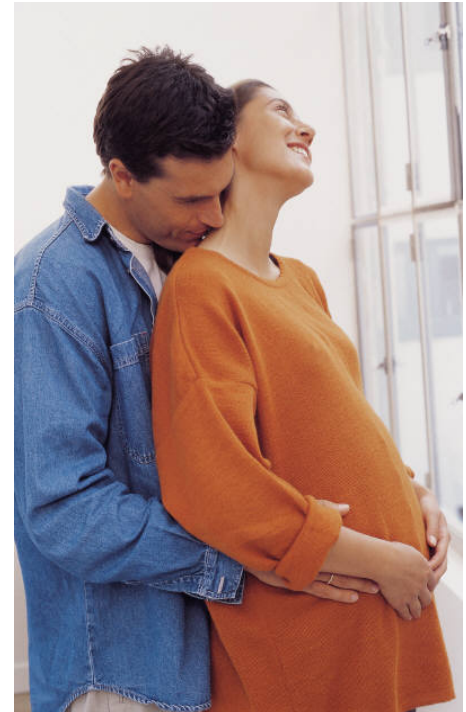
Iron Deficiency Anemia

- **Vit C, amino acids promote absorption**
- **Tea, veg. fiber increase uptake**
- **Gastric acid helps in solubility**



Iron Deficiency Anemia

- **Prevalence**
 - **Common nutritional deficiency worldwide**
 - **In U.S. found in women of childbearing age, infants, adolescents**
 - **In men, non-menstruating women**
 - **Blood loss**



Iron Deficiency Anemia

- **Categories**
 - **Iron deficiency without anemia**
 - **Iron deficiency anemia**

Iron Deficiency Anemia - Causes

- **Inadequate dietary iron**
- **Blood loss**
 - **Generally signifies pathological loss such as G.I. bleeding, vascular malformations, hookworm infestations, frequent blood donations**
- **~ 50% on renal dialysis show deficiency**

Iron Deficiency Anemia

- **Clinical features**
 - **Fatigue**
 - **Irritability**
 - **Headaches**
 - **Paresthesias**
 - **Pallor**
 - **Glossitis (a smooth red tongue)**
 - **Angular cheilitis**
 - **Koilonychia (spooning of the nails)**
 - **Pica (eating ice, clay, dirt)**

Iron Deficiency Anemia

- **Laboratory findings determine if:**
 - **Degree of anemia is mild to severe**
 - **Mean corpuscular volume is decreased**
 - **Red cell distribution width is decreased**

Iron Deficiency Anemia

- **Laboratory findings determine if:**
 - **White blood cells are normal**
 - **Platelets are normal to increased**
 - **Serum ferritin is low (12microg/L)**

Iron Deficiency Anemia

- **Management**
 - **Identify cause, correct if possible**
 - **Oral iron therapy**
 - **Adult dose 200 mg/day elemental iron**
 - **Pediatric dose 5mg/kg/day elemental**

Iron Deficiency Anemia

- **Management**
 - **Duration: Anemia usually corrected in 4-6 wks, continue for 3-6 mo, check serum ferritin concentration**

Iron Deficiency Anemia

- **Management (cont')**
 - **Iron dextran (INFeD®)**
 - **Iron sucrose (FERRLECIT®, VENOFER®)**
 - **Has less severe reaction than with iron dextran**

Thalassemia

- **Inherited disorders**
 - **<synthesis of a- or b- globin chains of Hb molecule**
 - **Occurs often in those of Mediterranean descent**
 - **Hallmark is insufficient a- or b- chain production**

A-Thalassemia

Genotype	Phenotype	Heme Findings
aa/aa	normal	normal
aa/a-	silent carrier	normal
aa/-- or a-/a-	A- Thalassemia trait	mild hypochromic in newborns Hb Barts (10%)

A-Thalassemia

Genotype	Phenotype	Heme Findings
a-/--	Hb H disease	in adults, Hb4 (5-40%) in newborns Hb Barts 20-40% hemolytic disease + ineffective erythropoiesis

A-Thalassemia

Genotype	Phenotype	Heme Findings
--/--	Hydrops fetalis	stillborn, anemic macerated fetus. Cord blood nearly 100% Hb Barts

A-Thalassemia

- **Prevalence of trait / symptoms**
 - **α -/ α - 7% Africans**
 - **α -/ α - common in S.E. Asia**
 - **MCV <78 dL; slight anemia**
 - **Hb Barts 2-10% in newborns**

A-Thalassemia

- **Prevalence of trait / symptoms (cont')**
 - **Diagnosis of exclusion (iron deficiency, B-Thalassemia, hereditary sideroblastic)**
 - **Do not confuse with iron deficiency**
 - **Do not treat with iron**

A-Thalassemia

- **Hemoglobin H disease**
 - **Hb H stains with cresyl blue**
 - **α^-/α^- , S.E. Asia**
 - **20-40% Hb Barts in newborns;
5-40% Hb H in adults**

A-Thalassemia

- **Hemoglobin H disease (cont')**
 - **Variable hemolytic anemia; splenomegaly**
 - **Ineffective erythropoiesis, iron-loading**

B-Thalassemia

- **Molecular defect/absent/reduced production of b-globin chains**
- **Broad spectrum of abnormalities**
- **Known as Mediterranean or Cooley's Anemia**
- **Fatal prior to transfusion and iron chelation therapy**

B-Thalassemia-Pathophysiology

- **> erythropoiesis, but ineffective**
- **Erythroid marrow expansion with bony deformities**
- **Progressive splenomegaly**
- **Extra-medullary hematopoiesis**
- **>iron absorption, progressive deposition in tissues**

B-Thalassemia

Clinical Features

- **Skeletal changes**
- **Extra-medullary hematopoiesis**
- **Growth retardation**
- **Delayed sexual maturation**
- **Myocardial iron overload**

B-Thalassemia

Clinical Features (cont')

- **Hepatic iron loading**
- **Pigmented gall stones**
- **Severe microcytic anemia, splenomegaly**

B-Thalassemia - Prognosis

- **No Rx-death by age 5 from infections, cachexia**
- **Episodic blood transfusions-Survival until 20s**
- **Aggressive blood transfusions-Death at age 20 from iron overload**
- **Aggressive blood transfusions + iron chelation-Prolonged survival**

B-Thalassemia - Management

- **Hypertransfusion in 2nd or 3rd yr to maintain Hb at 10g/dL**
- **Splenectomy**
- **Iron chelation after age 3**
- **Possibly bone marrow transplant**
- **Possibly increase synthesis of fetal Hb**

B-Thalassemia Minor

- **No clinical symptoms**
- **Labs**
 - **Mild to absent microcytic anemia**
 - **Peripheral blood smear shows microcytosis, hypochromia, targetting, basophylic stippling**
 - **Hb electrophoresis/quantitation: HbA >90%, HbA2 3.5-8.0%, HbF normal/>**

Sickle Cell Anemia

- **HbS: Sickle hemoglobin, most common heritable disease worldwide**
- **Prevalence**
 - **> tropical Africa/slave trade blacks**
 - **Some in Saudi Arabia, India**
 - **In U.S./Latin Am/Caribbean**
8% blacks with gene
 - **Note: Sickle cell trait not a disease**

Sickle Cell Anemia - Symptoms

- **Usually none until 6-12 months old**
- **Expression of HbSS limited during fetal and early postnatal life by HbF**
- **No single pattern of symptoms, but may include: pain and swelling in hands and feet, fatigue, paleness, shortness of breath, eye problems, yellowing of skin/eyes, delayed growth**

Sickle Cell Trait - Labs

- **Normal MCV, MCH**
- **Normal blood smear**
- **Normal reticulocyte count**
- **HbA 60%, HbS 40%**
- **Normal levels of HbA2, HbF**

Sickle Cell Anemia – Lab Values

- **Moderate-severe normocytic normochromic anemia by age 3 mo., persistent**
- **Av Hb 6.0-10.0g/dL**
- **Adults, mean MCV = 90**
- **Blood smears: sickled forms**
- **Howell-Jolly bodies reflect asplenia**
- **>WBC, platelets**

Sickle Cell Anemia

- **Diagnosis**
 - **Electrophoretic chromatographic studies**
 - **HbS predominant, HbF present, HbA2 normal**

Sickle Cell Anemia

- **Management**
 - **Folic acid 1mg PO qd**
 - **Hydroxyurea [generic] 15-35mg/kg PO**
 - **RBC transfusions**
 - **Stem cell transplant in children <16 yr, now for adults**

Aplastic Anemia - Symptoms

- **Bleeding in skin/mucous membranes**
- **Fatigue, fever, infection**
- **Mortality secondary to infection**
- **Pancytopenia**

Aplastic Anemia - Etiologies

- **Idiopathic in 50%**
- **Chemicals**
- **Chemotherapy**
- **Ionizing radiation**
- **Viral infection**
- **Leukemia**
- **Medications: Chloramphenicol, sulfa**
- **Auto-immune disorders**

Aplastic Anemia

- **Diagnosis**
 - **Bone marrow biopsy**
- **Epidemiology**
 - **2 / million worldwide**
 - **Prevalent in Orient**
 - **Peaks in late adolescence/early adulthood**

Aplastic Anemia

- **Pathogenesis**
 - **<Hematopoiesis**
 - **Autoimmunity**
- **Therapy**
 - **Supportive: blood product transfusions, antibiotics**
 - **Bone marrow transplant, immunosuppression**
 - **If severe: ATG + cyclosporine**

Megaloblastic Anemia

- **Cause**
 - **Impaired DNA synthesis,
cell division impaired,
cells enlarge**
 - **Vitamin B12 and folic acid deficiency**

Vitamin B12 Deficiency

- **What is normal**
 - **1-10mg total body Vitamin B12**
 - **Daily dietary requirement 2 micrograms**

Vitamin B12 Deficiency

- **Causes of deficiency**
 - **Pernicious anemia, Gastrectomy**
 - **Pancreatic insufficiency**
 - **GI bleeding, Vitamin B12 malabsorption**
 - **Exposure to nitrous oxide**
 - **Neurological findings**

Vitamin B12 Deficiency

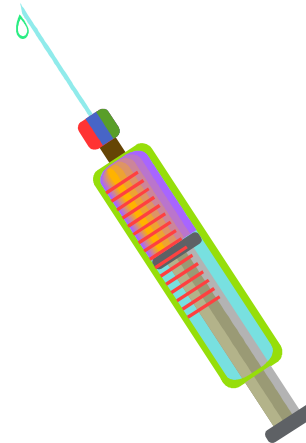
- **Diagnosis**
 - **Check B12 levels. If borderline, then check >serum or urine methylmalonic acid**
 - **LDH-1 isoenzyme > LDH-2**
 - **Elevated indirect bilirubin, serum iron, <haptoglobin**

Vitamin B12 Deficiency

- **Cause**
 - **Determine from clinical history/Schilling test**
 - **Schilling test**
 - **B12 test dose administered**

Vitamin B12 Deficiency

- **Treatment**
 - **I.M. Vitamin B12**
 - **Check for hypokalemia, cardiac arrhythmias, monitor serum potassium**



Vitamin B12 Deficiency

- **Treatment**
 - **Suggested I.M. injection schedule**
 - **1000mg qd I.M. or sub Q for 1-2 wks, then 1000mg I.M. each mo. for life, maintenance of 1000mg/day oral**



Total Body Folate Deficiency

- **Can cause megaloblastic anemia**
- **Adult has 5-10mg total body folate**
- **Usually accompanies Vitamin B12 deficiency**
- **Treatment**
 - **Folic acid therapy: oral 0.5-1.0mg/day**
 - **Give B12 also**

Glucose 6 Phosphate Dehydrogenase Deficiency (G6PD)

- **Hemolysis: Hallmark of hemolytic anemia, premature destruction of RBCs**
 - **Causes: acquired abnormal factors in intravascular environment, intrinsic RBC defects genetically determined**

Glucose 6 Phosphate Dehydrogenase Deficiency (G6PD)

- **G6PD deficiency: Hereditary hemolytic disorder of RBC enzyme defect, sex linked, affects males, carried by females**
- **Hb, RBC membranes at risk**

G6PD Dediciency

- **Clinical feature**
 - **Rapidly developing intravascular hemolysis**
- **Causative Agents**
 - **Infections, other illnesses**
 - **Drugs: antimalarials, sulfonamides, sulphones, other antibacterial agents, analgesics, anti-helminths, miscellaneous, fava bean**

G6PD Deficiency

- **Diagnosis**
 - **Between crises, blood count normal**
 - **During crisis, smear shows contracted and fragmented cells, “bite”/”blister” cells, Heinz bodies in reticulocytes**
 - **Do RBC assay, check G6PD level**

G6PD Deficiency

- **Treatment**
 - **Stop offending drug, maintain >urine output, blood transfusion, corticosteroids**

Summary

- **Definition of anemias**
- **Etiology, pathology, clinical features, diagnostic studies, and management of iron deficiency anemia, A- and B-Thalassemias, sickle cell anemia, aplastic anemia, and megaloblastic anemia**

Summary

- **Causes, diagnosis, and treatment of Vitamin B12 deficiency and total body folate deficiency**
- **Causes, clinical features, diagnosis and treatment of Glucose 6 Phosphate Dehydrogenase (G6PD) deficiency**